MULTIVARIATE SEGMENTATION OF BRAIN TISSUES BY FUSION OF MRI AND DTI DATA

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ABSTRACT

This paper proposes a method to improve brain-tissue segmentation, especially in *subcortical* region, by fusing the information in structural magnetic resonance (MR) images and diffusion tensor (DT) images in a sound statistical framework. The proposed method incorporates the information in DT images by parameterizing the space of diffusion tensors, in a principled and efficient manner, based on a set of *independent orthogonal invariants*. The proposed method couples the *Markov* tissue statistics of the structural-MR intensities with the tissue statistics of the DT invariants to define *multivariate*/joint probability density functions (PDFs) that differentiate brain tissues. The paper shows that while the information in DT images can allow improved differentiation between tissues in the subcortical region, which comprises anatomical structures having smooth (blob-like) shapes, it can produce unreliable results in the cortical regions that depict convoluted sulci/gyri. The proposed method exploits these characteristics of the images by introducing an appropriate anisotropic distance metric in the multivariate feature space.

Index Terms— Subcortical brain tissue segmentation, multivariate statistical analysis, MRI, DTI.

1. INTRODUCTION

Brain tissue segmentation in magnetic resonance (MR) images is a fundamental problem in clinical studies of brain structure and function. Some examples of such studies deal with measures of tissue/structure volumes, voxel-based morphometry, etc. Although many methods have been proposed in the last two decades [14, 15, 7, 1], segmentation of brain tissues, especially in the subcortical regions, remains a challenging task. This is primarily because of low intensity contrast in structural-MR images between the white matter (WM) and gray matter (GM) tissues in the subcortical regions that comprise structures such as the caudate, putamen, thalamus, etc. To compensate for this effect, typical approaches for segmenting subcortical structures must rely heavily on prior information, obtained from training data, in the form of tissue probability maps (probabilistic atlases) [5, 3] or shape priors [11, 8]. The availability of suitable training data, however, for most clinical datasets, limits the utility of such methods.

In recent years, diffusion tensor (DT) MR imaging has gained significant popularity because of its ability to measure the anisotropic diffusion of water in structured biological tissue. It has the ability to differentiate between several anatomical structures of the brain, especially in the WM, that was impossible with structural-MR imaging. On the other hand, DT images also contain information to differentiate between brain tissues; WM shows highly anisotropic diffusion, cerebrospinal fluid (CSF) shows large mean diffusivity, and GM shows neither. In the subcortical regions, DT images have sufficient information to discriminate between the WM and GM tissues; much more so than structural-MR images. In this way, the information in DT images can be exploited to improve brain tissue segmentation.

This paper proposes a method to improve segmentation of brain tissues, especially in subcortical region, by fusing the information in structural-MR images and DT images in a sound statistical segmentation framework. The proposed method incorporates the information in DT images by fitting DT models at each voxel and, subsequently, parameterizing the space of diffusion tensors, in a principled and efficient manner, based on a set of orthogonal independent invariants [6]. Structural-MR images are modeled using a Markov random field (MRF) [1]. The proposed method couples the Markov tissue statistics of the structural-MR intensities with the tissue statistics of the DT invariants to define multivariate probability density functions (PDFs) for brain tissues. The multivariate PDFs are modeled using a nonparametric density estimation scheme. The paper shows that while the DT images can improve differentiation between tissues in the subcortical region, which comprises structures having smooth (blob-like) shapes, they can produce unreliable results in the cortical regions that depict convoluted sulcul/gyral structures. The proposed method exploits these characteristics of the images by introducing an appropriate anisotropic distance metric in the multivariate feature space.

2. BACKGROUND

A class of approaches for segmenting subcortical structures rely on probabilistic atlas priors created using structural-MR images [5, 3]. Such approaches rely on the accuracy of the manual segmentations of subcortical structures in the training data that generated the probabilistic atlas as well as the accuracy of the registration method, to map the template space to the subject space, in the absence of strong intensity contrast in the subcortical tissues.

Barra and Boire [2] present an information-fusion technique that extracts prior information, comprising morphological and topological properties of tissue structures, from structural-MR images and experts. These information channels are fused in a fuzzy-logic framework that weights the information in different channels based on an evaluation of its accuracy. Another class of approaches rely on deformable shape models [11, 8] that employ a shape-based

prior, i.e. a model for the statistical distribution of shapes in some parametric space, in a Bayesian segmentation scheme.

Some recent approaches [10, 4, 9] incorporate the information in DT images to aid in the accurate segmentation of subcortical tissue structures. Liu et al. [10] proposed to employ the mean apparent diffusion coefficient (ADC) to separate the CSF from the WM and GM tissues and to employ the fractional anisotropy (FA) to separate the WM from the GM and CSF tissues. They compute the final tissue segmentations as defined by the overlap of the segmentations, obtained independently, from the MR and DT images. In recent work [9], Liu et al. improve their approach by employing an expectation-maximization based algorithm [13] to combine the segmentations, obtained *independently*, using 7 different images of tensor invariants (invariant to tensor orientation) and the structural-MR image. Employing 7 tensor derivatives, however, may lead to redundant usage of information because tensor invariants themselves have only 3 degrees of freedom.

The proposed method improves upon the previous work in several ways. First, it proposes a *data-driven* technique to segment subcortical tissue structures by incorporating the information in DT images, in contrast to prior-driven approaches. It shows that reliable subcortical segmentations can be obtained by using only 2 tensor invariants, which form an orthogonal and independent basis of a subspace of the 6-dimensional space of tensors. Two examples are [6]: (i) the space formed by tensor trace and the deviatoric-tensor norm, and (ii) the space formed by the tensor norm and the FA. The third invariant is the tensor mode that is typically extremely noisy and may *not* be a reliable source of information [6]. The orientation of the tensor does *not* convey important information to differentiate brain tissues. In this way, the proposed method optimally incorporates the information in DT images for multivariate segmentation. Moreover, incorporating several redundant sources of information during the multivariate analysis may reduce the accuracy of the segmentation by introducing more uncertainty/variability in the tissue statistics.

This paper also shows that imaging artifacts (e.g. low resolution, eddy-current distortion) in typical DT-imaging acquisitions may reduce the efficacy of the tensor measures to differentiate the WM and GM in the cortical region. This concern was also raised by Liu et al. [10]. Structural-MR images, on the other hand, provide reliable intensity contrast to enable accurate tissue differentiation in the cortex. Artifacts introduced by DT imaging may also compromise the accuracy of the registration of the DT and structural-MR images in the cortical region [10]. The proposed method exploits this information to spatially adapt the influence of the two modalities in computing the optimal segmentation.

3. MULTIVARIATE BRAIN TISSUE SEGMENTATION

For fusing the information in the structural-MR and DT images, the b0 image associated with the diffusion weighted (DW) images is linearly aligned to the structural-MR image. The DW images are then resampled based on this alignment in order to equate their spatial resolution to that of the structural-MR image. The DW images are then used to fit a DT model at each voxel.

For the segmentation framework, we impose a random-field statistical model on structural-MR and DT images [1]. This implies that the value at each voxel v is an instance of a random variable. We denote the random variables at each voxel in the structural-MR image by uppercase letters S_v and those in the DT image by D_v; the values in the images at those voxels are denoted by lowercase letters s_v and d_v, respectively. From the DT image, we construct images

of tensor norm and FA with the underlying random variables at each voxel as N_v and F_v, respectively.

We model context dependence, at each voxel v, in the brain region in the structural-MR image using a MRF with a first-order neighborhood (6 nearest neighbors of a voxel), namely N_v. Thus, the Markov PDF that dictates the statistical characteristics at each voxel v is given by $P(\{S_v\}_{v \in N_v})$. Fusing the information from the DT image, at each voxel v, the multivariate/joint PDF becomes $P(\{S_v\}_{v \in N_v}, F_v, N_v)$. We assume that the Markov PDFs for all voxels belonging to a particular tissue are equivalent and that the MRF is piecewise ergodic. We denote the multivariate PDF for tissue k by the short hand $P_k(\mathbf{Z})$ where the random vector $\mathbf{Z} = \{\{S_v\}_{v \in N_v}, F_v, N_v\}$. In this paper k takes $K = 3$ different values that correspond to the labels for WM, GM, and CSF.

To define the optimal tissue segmentation, first consider a discrete random variable $L : \mathcal{V} \rightarrow \mathcal{Z}$, where $\mathcal{Z}$ is the set of integers, that maps each voxel $v \in \mathcal{V}$ to the class it belongs to; i.e., $L_v = k$ if voxel v belongs to tissue k. Let $\{\mathcal{V}_k\}_{k=1}^K$ denote a mutually-exclusive and collectively-exhaustive decomposition of the brain voxels $\mathcal{V}$ into K regions.

We model the multivariate tissue PDFs using *Parzen-window* nonparametric density estimation. For the piecewise stationary-ergodic MRF, this gives the multivariate probability that the set of values z_v in the structural-MR, FA, and tensor-norm images at voxel v belong to tissue k as

$$P_k(\mathbf{z}_v) \approx \frac{1}{|\mathcal{A}|} \sum_{u \in \mathcal{U}} G(\mathbf{z}_v; \mathbf{z}_u, \Psi), \qquad (1)$$

where the set $\mathcal{U}$ is a small subset of $\mathcal{V}_k$ chosen randomly in the area of the brain surrounding voxel v, $G(\cdot; \mu, \Psi)$ is a Gaussian kernel with mean μ and a diagonal covariance matrix Ψ. More details about this scheme can be found in [1].

We now define the optimal segmentation. Using the set of multivariate tissue PDFs $\{P_k(\mathbf{Z})\}$ for the K tissues, we can define a joint PDF $P(L, \mathbf{Z})$ between the label values and the image values. During the creation of the image, at each voxel v, an instance $(l_v, \mathbf{z}_v)$ was drawn from the multivariate PDF. What was observed, however, were only the image values $\mathbf{z}_t$. The label values l_t must be inferred from the image data in conformation with the multivariate image model. We define the optimal segmentation as the one that maximizes the *mutual information* between L and $\mathbf{Z}$, namely $I(L, \mathbf{Z})$. Intuitively, the mutual information between two random variables quantifies the degree of functional dependence between them. For functionally-dependent random variables, each variable uniquely determines the other, and the mutual information is maximized. On the other hand, independent random variables convey no information about each other, and their mutual information is zero (minimal). A desirable segmentation is one in which the image values provide the most information about the class labels. Likewise, knowing the voxel class should provide the most reliable estimate of the voxel neighborhood.

We adopt an iterative steepest descent scheme for the optimization. We obtain the initial segmentation following a template-based segmentation approach using the probabilistic tissue atlas publicly available at the ICBM website [1]; we linearly align the structural-MR image to the ICBM template and map the tissue probabilities from the template space to the given image. This strategy also implicitly strips all the non-brain structures from the MR images.

Given a segmentation, $\{\mathcal{V}_k^n = \{v \in \mathcal{V} : L_v^n = k\}\}_{k=1}^K$ at iteration n, the optimization iterates, until convergence, as follows:

[1] http://www.loni.ucla.edu/ICBM

1. For $k = 1, 2, 3$, and $\forall v \in \mathcal{V}$, estimate $P_k^n(\mathbf{z}_t)$ nonparametrically, as described in (1).

2. Update the label at each voxel to increase $I(L, \mathbf{Z})$ using the rule: $L_v^{n+1} = \arg\max_k P_k^n(\mathbf{z}_v)$.

The algorithm typically convergences in less than 4 iterations.

   As described before, in the cortical region, typical DT imaging resolutions and artifacts may reduce the efficacy of the tensor measures to distinguish between the WM and GM [10]. Structural-MR images, on the other hand, do provide reliable intensity contrast to enable accurate tissue differentiation. The proposed method exploits this behavior by introducing a *spatially-varying* anisotropic distance metric in the multivariate feature space. We use the ICBM template space to approximate a spatially-varying mask $m(v)$ that roughly defines the subcortical region; $m(v) = \alpha$ for voxels v inside the subcortical region and $m(v)$ smoothly changes to $(1 - \alpha)$ as the voxel location moves out of the cortical region. We then replace Ψ in (1) by $\Psi_v = \lambda_v \Psi$, where λ_v is a vector whose i-th component equals $m(v)$ if the i-th component of $\mathbf{z}_v$ corresponds to a tensor invariant or equals $(1 - m(v))$ if the i-th component of $\mathbf{z}_v$ corresponds to the structural-MR intensity. In this paper, we set $\alpha = 0.9$ (this free parameter can be empirically tuned based on the relative quality of the images of the two modalities in a particular dataset). In this way, the tensor invariants have a stronger effect in determining the label for a voxel inside the subcortical regions compared to a voxel outside the cortical region. At the same time, the tissue labels $\mathcal{U} \subset \mathcal{V}_k$ in the *entire* brain contribute in correctly estimating the multivariate tissue statistics both inside and outside the subcortical region. Thus, the information in both the structural-MR and DT modalities complements each other to ease tissue differentiation.

   The implementation of the proposed method relies on the Insight Toolkit (ITK) [2]. This paper employs a novel algorithm that incorporates careful approximations in the modeling strategy in order to obtain an order-of-magnitude speedup and reduce memory usage, as compared to the ITK implementation in [1], without any perceptible reduction in performance. The running time for the implementation for the images in this paper is about 6 minutes per iteration using a standard Pentium 2.66 GHz machine. The method's algorithmic complexity is linear in the number of brain voxels.

4. MR IMAGE ACQUISITION

The images used in this paper were acquired using a 1.5T Siemens scanner for a clinical study [12]. The structural-MR image was acquired using a T1-weighted magnetization-prepared rapid gradient echo (MP-RAGE) sequence with a slice thickness of 1 mm, yielding 160 sagittal slices with an in-plane resolution of 1x1 mm. A single-shot, spin-echo, DT echo-planar imaging (EPI) sequence was used to get the DT images: 1 image without diffusion gradients (b = 0 s/mm^2) followed by 6 images acquired using noncollinear diffusion-encoding directions isotropically distributed in space (b = 1000 s/mm^2), a *slice thickness of 5 mm* yielding 20 axial slices with an in-place resolution of 2x2 mm. This sequence allowed a partial brain coverage that covered the more superior portions of the brain; from the top of the brain to the superior third of the cerebellum.

5. RESULTS

Figures 1(a) and (b) show two corresponding axial slices, in the *subcortical* region, of the structural-MR and DT images, respectively,
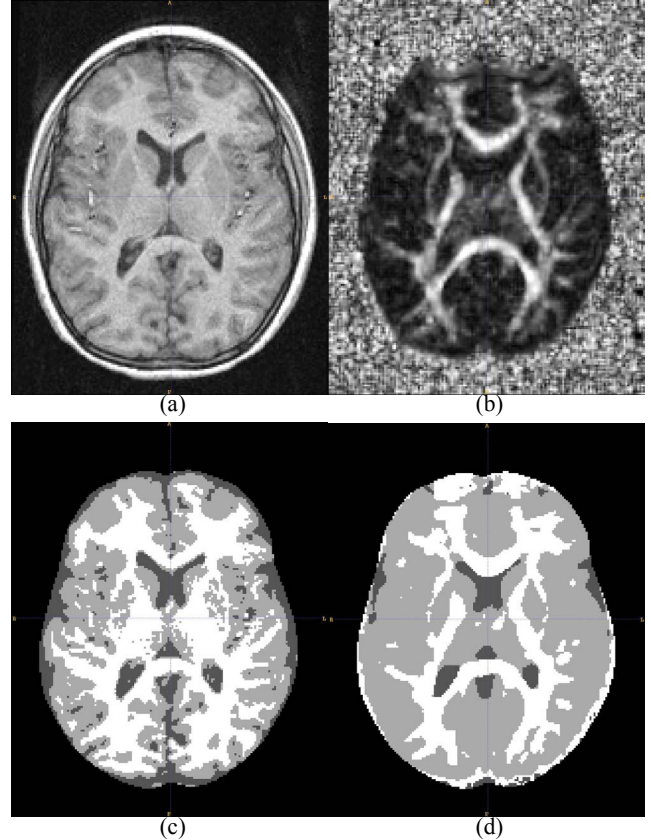
[2] http://www.itk.org

Fig. 1. Axial slices showing *subcortical* regions in the: (a) MR image, (b) FA image, (c) segmentation using the MR image alone, and (d) segmentation using the orthogonal tensor invariants alone.

that shows the ability of DT data to differentiate subcortical tissue structures. Figures 1(c) and (d) show the segmentations, for the same axial slice, obtained by using the the two modalities *independently*.

   Figures 2(a) and (b) compare the information present in the two modalities in the *cortical* brain region, where the structural-MR image provides much stronger contrast between the convoluted tissue structures. Figures 2(c) and (d) show the segmentations obtained by using the the two modalities *independently*.

   Figures 3(a) and (b) show the tissue segmentation using the proposed *multivariate* segmentation method in the subcortical and cortical regions, respectively. Figure 3(a) shows significant improvement in the subcortical segmentation, as compared to the segmentation using the structural-MR image alone (Figures 1(c)), that enhances the differentiation between the deep-GM structures (caudate, putamen, and thalamus) and the adjoining WM. Similarly, Figure 3(b) shows that the multivariate method retains the same accuracy of tissue differentiation in the cortical region, as obtained with the structural-MR image alone (Figures 2(d)).

6. CONCLUSION

The results in this paper demonstrate the potential of the proposed method for data-driven segmentation of subcortical tissue structures, in contrast to typical prior-driven training-intensive schemes. The only weak prior anatomical knowledge incorporated in the proposed method is through the smoothed mask of the subcortical region in
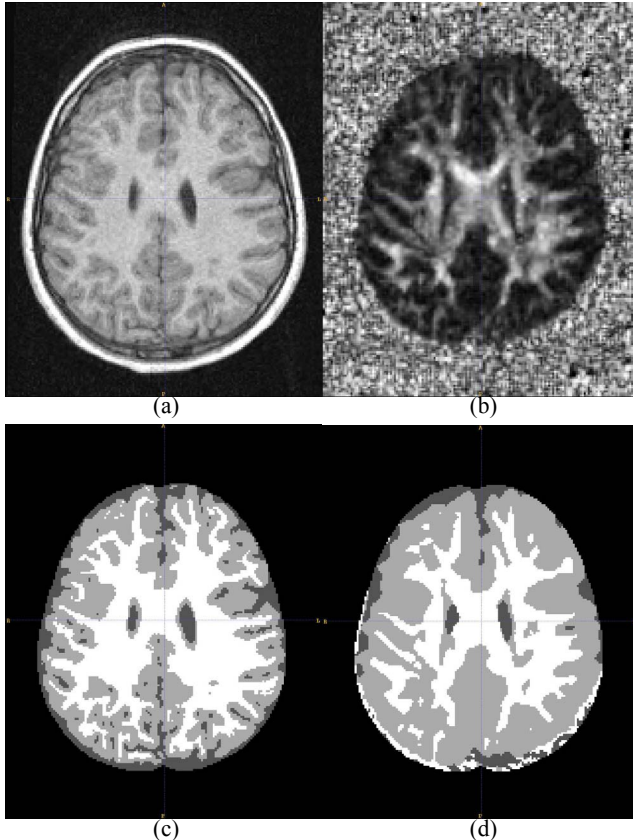
Fig. 2. Axial slices showing *cortical* regions in the: (a) MR image, (b) FA image, (c) segmentation using the MR image alone, and (d) segmentation using the orthogonal tensor invariants alone.

the ICBM template. Experiments show that the segmentation result is robust to minor inaccuracies in the definition of this smooth mask. Future work will focus on better quantitative validation of the proposed method and its application in clinical studies.
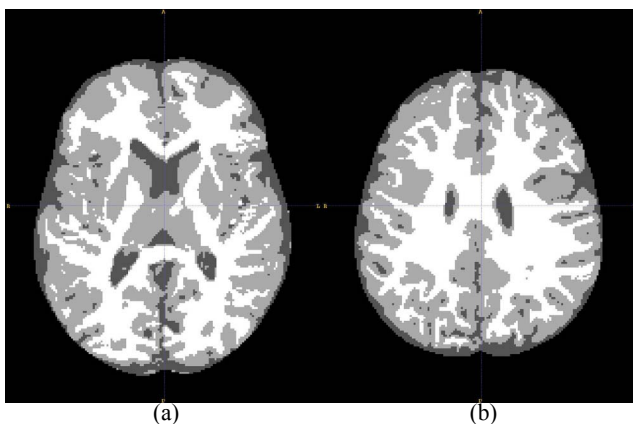

Fig. 3. Axial slices showing the multivariate segmentation in the (a) subcortical and (b) cortical region. The segmentation method coupled/fused a nonparametric MRF model on the structural-MR image and a nonparametric model for orthogonal tensor invariants.

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